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CORRESPONDENCE

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# Human Herpesvirus 8 and Renal Transplantation

*To the Editor:* In their discussion, Regamey et al. (Nov. 5 issue)[1] suggest that in regions where human herpesvirus 8 (HHV-8) is not endemic, transplantation-associated Kaposi's sarcoma is often transmitted from the donor. Between January 1993 and December 1995, we checked 166 consecutive patients for HHV-8 antibodies, examining all serum samples collected before kidney transplantation. Antibodies to a latent nuclear antigen (LNA-1) of HHV-8 were detected with an immunofluorescence assay in a primary effusion cell line (BCP-1) latently infected with HHV-8 but not with the Epstein–Barr virus. The immunofluorescence assay was performed as previously described[2] with a serum dilution of 1:100.

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Of the 166 patients, 16 (9.6 percent) had antibodies to HHV-8 in serum samples obtained before transplantation. Antibodies to HHV-8 were present in the serum of 7 percent of patients from France (4 of 57), 17 percent of patients from French overseas departments (1 of 6), 10 percent of patients from North Africa (6 of 60), 21 percent of patients from sub-Saharan Africa (3 of 14), 15 percent of patients from Italy (2 of 13), and 0 percent of patients from other countries (0 of 16). Four of these 16 patients died or resumed dialysis between one and eight months after renal transplantation. The other 12 seropositive patients were followed for at least three years after transplantation and had functional grafts. Kaposi's sarcoma developed in 4 of these 12 patients (33 percent) between 8 and 30 months after transplantation: 2 patients were from sub-Saharan Africa and 1 patient each was from French overseas departments and North Africa. Kaposi's sarcoma did not develop in any of the 150 patients who were seronegative for HHV-8 before transplantation.

HHV-8 infection is not endemic in France, since the prevalence of antibodies to HHV-8 among French blood donors is only 2 percent.[3] The seroprevalence of HHV-8 before transplantation in our patients was similar to that in the study by Regamey et al. However, in our patients, Kaposi's sarcoma was observed

only in those who were infected with HHV-8 before transplantation. These results suggest that in our patients, Kaposi's sarcoma was associated with a reactivation of HHV-8 infection due to immunosuppression and was not associated with primary HHV-8 infection. Similar results were reported by Parravicini et al., who found that 10 of 11 Italian kidney-transplant recipients with Kaposi's sarcoma had had a positive serologic test for HHV-8 before transplantation.[4] Ongoing studies of large series of transplant recipients with Kaposi's sarcoma are required to explain these controversial data.

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*To the Editor:* Neither of the 2 patients with transplantation-associated Kaposi's sarcoma described by Regamey et al. had antibodies to HHV-8 at the time of transplantation, in contrast to the results of an Italian series, in which 10 of 11 such patients were seropositive for HHV-8.[1] To account for the discrepancy, Regamey et al. suggested that post-transplantation Kaposi's sarcoma is primarily due to the reactivation of HHV-8 in populations with a high prevalence of HHV-8 and to primary infections in populations with a low prevalence of infection. We have examined this hypothesis in recipients of solid-organ allografts at Toronto Hospital; in this population the risk of Kaposi's sarcoma is 5 percent among recipients of Italian or Greek background and 0.2 percent among those of other ethnic backgrounds.[2]

Serum samples were obtained before transplantation from one Italian patient and two non-Italian white patients in whom Kaposi's sarcoma developed after transplantation and from six controls matched for allograft type and ethnic background. HHV-8 antibody testing was performed with a whole-virus enzyme-linked immunoassay (ABI HHV-8 ELISA, Advanced Biotechnologies, Columbia, Md.) and an immunofluorescence assay for antibody to latent antigens.[3] Both assays showed that the Italian patient was seropositive for HHV-8 at the time of transplantation, whereas the two non-Italian patients were seronegative; one of the six controls was seropositive on both assays, and another was positive on the

immunofluorescence assay only.

Although the epidemiology of asymptomatic HHV-8 infection is still being defined, a recent survey found HHV-8 antibodies in 14 percent of Italian blood donors.[4] Our data support the hypothesis that the epidemiology of transplantation-associated Kaposi's sarcoma differs between populations with a high prevalence of HHV-8 seropositivity and those with a low prevalence of seropositivity.

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The authors reply:

*To the Editor:* There is convincing evidence that Kaposi's sarcoma is associated with HHV-8 infection. HHV-8 DNA can be detected in tissue samples, and antibodies to HHV-8 are found in all forms of Kaposi's sarcoma, including transplantation-associated Kaposi's sarcoma.[1,2] However, it is still unclear whether Kaposi's sarcoma after transplantation is due to the reactivation of HHV-8 as a result of immunosuppression or to primary HHV-8 infection. In our study, we showed that HHV-8 can be transmitted by transplanted organs. Two patients in whom Kaposi's sarcoma developed after transplantation were HHV-8–seronegative at the time of transplantation, suggesting that infection was transmitted through donor organs. Francès and colleagues describe four patients with Kaposi's sarcoma who were seropositive before transplantation, whereas Rabkin and coworkers and Parravicini et al.[3] describe Kaposi's sarcoma in patients with antibodies to HHV-8 before transplantation and in those

without antibodies. It therefore seems highly likely that Kaposi's sarcoma can develop in transplant recipients after either primary infection with HHV-8 (e.g., transmitted from the donor through the transplant) or reactivation of the virus. Rabkin and coworkers support our hypothesis that in a population with a low prevalence of HHV-8, transplantation-associated Kaposi's sarcoma may develop after the transmission of the virus from the donor through the allograft. However, we agree that further studies are necessary to prove our hypothesis.

Although the direct association between HHV-8 infection and Kaposi's sarcoma has been established, other virus-associated or host-associated cofactors may be required for the development of Kaposi's sarcoma in addition to the impairment of the immune response.[4] Post-transplantation lymphoproliferative disorders mainly develop in patients with new Epstein–Barr virus infections or in patients with high levels of Epstein–Barr virus in the peripheral blood. We are currently studying patients with HHV-8 viremia after transplantation and also searching for possible cofactors for the development of Kaposi's sarcoma. Patients with persistent HHV-8 viremia after primary HHV-8 infection or a reactivation of infection as a result of immunosuppression might be at increased risk for Kaposi's sarcoma.

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